Complete Summary

GUIDELINE TITLE

Recommendations for the prevention and treatment of glucocorticoid-induced osteoporosis: 2001 update.

BIBLIOGRAPHIC SOURCE(S)

Recommendations for the prevention and treatment of glucocorticoid-induced osteoporosis: 2001 update. American College of Rheumatology Ad Hoc Committee on Glucocorticoid-Induced Osteoporosis. Arthritis Rheum 2001 Jul;44(7):1496-503. [54 references]

GUIDELINE STATUS

This is the current release of the guideline. This guideline updates a previously released guideline (Recommendations for the prevention and treatment of glucocorticoid-induced osteoporosis. American College of Rheumatology Task Force on Osteoporosis Guidelines. Arthritis Rheum 1996 Nov;39[11]:1791-801).

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Osteoporosis

GUIDELINE CATEGORY

Prevention
Treatment

CLINICAL SPECIALTY

Endocrinology
Family Practice
Internal Medicine
Obstetrics and Gynecology
Pulmonary Medicine
Rheumatology

INTENDED USERS

Physicians

GUIDELINE OBJECTIVE(S)

To educate and update physicians on the prevention and treatment of glucocorticoid-induced osteoporosis

TARGET POPULATION

Adults who are or will be receiving glucocorticoids

INTERVENTIONS AND PRACTICES CONSIDERED

Prevention and Treatment

1. Bone mineral density measurement at lumbar spine and/or hip
2. Calcium and vitamin D supplementation
3. Replacement of gonadal sex hormones
4. Bisphosphonates (alendronate and risedronate)
5. Calcitonin
6. Lifestyle modification, such as smoking cessation or avoidance, and reduction of alcohol consumption if excessive
7. Instruction in weight-bearing physical exercise

Note: Anabolic agents, such as fluoride are considered but not recommended.

MAJOR OUTCOMES CONSIDERED

- Bone mineral density changes
- Rates of vertebral fracture reduction

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Not stated

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Not stated

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Not applicable

METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Not stated

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Not stated

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Excerpted by the National Guideline Clearinghouse (NGC):

Glucocorticoid-induced bone loss should be prevented, and if present, should be treated (see the section titled "Recommendations for the Prevention and Treatment of Glucocorticoid-induced Osteoporosis," below). Supplementation with calcium and vitamin D at a dosage of 800 IU/day, or an activated form of vitamin D (e.g., alfacalcidiol at 1 micrograms/day or calcitriol at 0.5 micrograms/day), should be offered to all patients receiving glucocorticoids, to restore normal calcium balance. This combination has been shown to maintain bone mass in patients receiving long-term low-to-medium-dose glucocorticoid therapy who have normal levels of gonadal hormones. However, while supplementation with calcium and vitamin D alone generally will not prevent bone loss in patients in whom medium-to-high-dose glucocorticoid therapy is being initiated, supplementation with calcium and an activated form of vitamin D will prevent bone loss. There are no data available to support any conclusion about the antifracture efficacy of the combination of calcium supplementation plus an activated form of vitamin D.

Antiresorptive agents are effective in the treatment of glucocorticoid-induced bone loss. All of these agents either prevent bone loss or modestly increase lumbar spine bone mass and maintain hip bone mass. While there are no randomized controlled trials of prevention of glucocorticoid-induced bone loss or radiographic vertebral fracture outcomes with hormone replacement therapy or testosterone, patients receiving long-term glucocorticoid therapy who are hypogonadal should be offered hormone replacement therapy. The bisphosphonates are effective for both the prevention and the treatment of glucocorticoid-induced bone loss. Large studies have demonstrated that bisphosphonates also reduce the incidence of radiographic vertebral fractures in postmenopausal women with glucocorticoid-induced osteoporosis. Treatment with a bisphosphonate is recommended to prevent bone loss in all men and postmenopausal women in whom long-term glucocorticoid treatment at $\geq$5 mg/day is being initiated, as well as in men and postmenopausal women receiving long-term glucocorticoids in whom the bone mineral density T-score at either the lumbar spine or the hip is below normal.

While there is little information on the prevention or treatment of bone loss in premenopausal women, these women, too, may lose bone mass if they are being treated with glucocorticoids, so prevention of bone loss with antiresorptive agents should be considered. If bisphosphonate therapy is being considered for a premenopausal woman, she must be counseled regarding use of appropriate contraception.

The therapies to prevent or treat glucocorticoid-induced bone loss should be continued as long as the patient is receiving glucocorticoids. Data from large studies of anabolic agents (e.g., parathyroid hormone) and further studies of combination therapy in patients receiving glucocorticoids are eagerly awaited so additional options will be available for the prevention of this serious complication of glucocorticoid treatment.

Recommendations for the Prevention and Treatment of Glucocorticoid-induced Osteoporosis

Patients beginning therapy with glucocorticoid (prednisone equivalent of $\geq$5 mg/day) with plans for treatment duration of $\geq$3 months:

- Modify lifestyle risk factors for osteoporosis:

    - Smoking cessation or avoidance
    - Reduction of alcohol consumption if excessive
- Instruct in weight-bearing physical exercise
- Initiate calcium supplementation
- Initiate supplementation with vitamin D (plain or activated form)
- Prescribe bisphosphonate (use with caution in premenopausal women)

Patients receiving long-term glucocorticoid therapy (prednisone equivalent of ≥5 mg/day):

- Modify lifestyle risk factors for osteoporosis:
    - Smoking cessation or avoidance
    - Reduction of alcohol consumption if excessive
- Instruct in weight-bearing physical exercise
- Initiate calcium supplementation
- Initiate supplementation with vitamin D (plain or activated form)
- Prescribe treatment to replace gonadal sex hormones if deficient or otherwise clinically indicated
- Measure bone mineral density (BMD) at lumbar spine and/or hip
  If bone mineral density is not normal (i.e., T-score below -1), then:
    - Prescribe bisphosphonate (use with caution in premenopausal women)
    - Consider calcitonin as second-line agent if patient has contraindication to or does not tolerate bisphosphonate therapy
- If bone mineral density is normal, follow up and repeat bone mineral density measurement either annually or biannually

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is not specifically stated for each recommendation.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Overall, the guideline recommendations may help to effectively prevent and treat glucocorticoid-induced bone loss and reduce the incidence of osteoporotic fractures associated with glucocorticoid use.

Supplementation with calcium and vitamin D has been shown to maintain bone mass in patients receiving long-term low-to-medium-dose glucocorticoid therapy who have normal levels of gonadal hormones.

Antiresorptive agents are effective in the treatment of glucocorticoid-induced bone loss. All of these agents either prevent bone loss or modestly increase lumbar spine bone mass and maintain hip bone mass.

The bisphosphonates are effective for both the prevention and the treatment of glucocorticoid-induced bone loss. Large studies have demonstrated that bisphosphonates also reduce the incidence of radiographic vertebral fractures in postmenopausal women with glucocorticoid-induced osteoporosis.

POTENTIAL HARMS

It should be noted that if activated forms of vitamin D are used, especially in patients who are just beginning glucocorticoid therapy, these patients should be carefully monitored for the development of hypercalcemia and hypercalciuria; if these adverse events develop, the dosage of the activated vitamin D supplement should be reduced.

All patients receiving long-term glucocorticoid treatment should be assessed for hypogonadism, and when present, this should be corrected if possible.

It is important to emphasize that if testosterone replacement therapy is to be used in a hypogonadal man, the patient should be adequately assessed for the possibility of prostate cancer, with a digital rectal examination and measurement of prostate-specific antigen at baseline and annually thereafter. Prostate cancer is an absolute contraindication to testosterone replacement therapy.

QUALIFYING STATEMENTS

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The American College of Rheumatology Committee on Glucocorticoid-Induced Osteoporosis emphasizes that the recommendations are not fixed, rigid mandates and recognizes that the final decision concerning the treatment regimen for an individual patient results from an informed discussion between the patient and his or her health care provider.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Staying Healthy

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

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ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

1996 Sep 3 (updated 2001)

GUIDELINE DEVELOPER(S)

American College of Rheumatology - Medical Specialty Society

SOURCE(S) OF FUNDING

American College of Rheumatology (ACR)

GUIDELINE COMMITTEE

Committee on Glucocorticoid-Induced Osteoporosis

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Committee on Glucocorticoid-Induced Osteoporosis: Lenore Buckley, MD, MPH; Maria Greenwald, MD; Marc Hochberg, MD, MPH; Nancy Lane, MD; Stephen Lindsey, MD; Stephen Paget, MD; Ken Saag, MD, MSc; Lee Simon, MD

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Dr. Hochberg has received grant and/or clinical research support form Merck & Co. and Aventis Pharmaceuticals; has served as a consultant to Aventis Pharmaceuticals, Biomatrix, Eli Lilly & Co., Merck & Co., NEGMA Laboratories, Procter & Gamble, Roche Pharmaceuticals, Sanofi-Synthelab, and Wyeth Ayerst; and is a stock shareholder (not major equity) in Jonnson & Johnson, Eli Lilly & Co., Merck & Co., Procter & Gamble and Schering Plough. Dr. Saag has received grant support from Merck & Co., Aventis Pharmaceuticals, and Wyeth Ayerst; has served as a consultant to Merck & Co., Procter & Gamble, and Eli Lilly & Co.; and has served as a speaker for Merck & Co., Procter & Gamble, and Aventis

Pharmaceuticals. Dr. Simon has served on medical advisory boards, related to bone disease, of Merck & Co., Eli Lilly & Co., and Aventis Pharmaceuticals; has received grant and/or contract support from Bristol-Myers Squibb, Procter & Gamble, La Jolla Pharmaceuticals, Amgen, Novartis Pharmaceuticals, AstraZeneca Pharmaceuticals, Forrest Pharmaceuticals, Abgenix, Vertex, G.D. Searle & Co., and Pharmacia; has served as a consultant to Abgenix, Aventis Pharmaceuticals, AstraZeneca Pharmaceuticals, Pharmacia, Immunex, Procter & Gamble, Eli Lilly & Co., Merck & Co., Merck-Medco, Caremarke, Forest Pharmaceuticals and Pfizer; and has served as a speaker for Centocor, Pharmacia, Pfizer, Merck & Co., and Aventis Pharmaceuticals.

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GUIDELINE AVAILABILITY

Electronic copies: Available from the American College of Rheumatology (ACR) Web site.

Print copies: Available from the American College of Rheumatology, 1800 Century Place, Suite 250, Atlanta, GA 30345.

AVAILABILITY OF COMPANION DOCUMENTS

The following is available:

- Guidelines for the development of practice guidelines. Atlanta (GA): American College of Rheumatology, 1998. 4 p. Electronic copies are available from the American College of Rheumatology (ACR) Web site.

Print copies: Available from the American College of Rheumatology, 1800 Century Place, Suite 250, Atlanta, GA 30345.

PATIENT RESOURCES

None available

NGC STATUS

This summary was completed by ECRI on October 17, 2001. The information was verified by the guideline developer as of May 8, 2002.

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